



CASE REPORT

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Erythropoietin Induced Atypical Erythema Multiforme in a patient with chronic kidney disease– a rare presentation

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ARTICLE INFO ABSTRACT



Received 01 May 2025;
Revised 11 June 2025;
Accepted 11 August 2025.

Keywords:

Adverse drug reaction,
Rash, Erythropoietin-
stimulating agents

Introduction: Erythema multiforme is a hypersensitivity reaction to different antigenic stimuli, mostly due to infections followed by drugs. Erythropoietin-induced Erythema Multiforme is one of the rarest serious adverse effects seen till date.

Case Presentation: The patient was a case of Anaemia in Chronic Kidney disease and was advised Inj Erythropoietin 4000 IU, subcutaneously after every 15 days. After taking 2nd dose of Inj Erythropoietin, the patient developed erythematous polymorphous eruptions over palms, hands, abdomen. Following which the patient developed fever and athralgia. A diagnosis of Erythropoietin Induced Erythema Multiforme was made. Patient recovered completely over few weeks. The adverse event was reported to the regional Pharmacovigilance Centre.

Management: Erythropoiesis Stimulating Agents (ESA) are used to treat anaemia in Chronic Kidney Disease. Drug Induced Erythema Multiforme is a delayed Type IV hypersensitivity reaction, associated with prodromal symptoms such as Fever, cough, difficulty in breathing, joint pain and swelling. Patient improves with IV corticosteroids, antihistamines and emollients.

Conclusion: Erythropoietin should be offered meticulously in patients with anaemia in CKD, considering its benefit in terms of quality of life and physical function. Extreme caution to be taken while prescribing Erythropoietin therapy in patients with history of stroke, or any hypersensitivity reaction.

An official publication of the Global Pharmacovigilance Society.

Introduction

Epoetin alfa (Erythropoietin), also known as human recombinant erythropoietin, is extensively used to treat anaemia in different forms that are associated with chemotherapy, HIV treatment, chronic renal disease, and other medical disorders.

The medication is usually well tolerated; nevertheless, among the more frequent side effects are pyrexia,

localised skin responses, and elevated blood pressure. Prescribers need to be aware of possible rare adverse effects, such as hypersensitivity reactions, elevated risk of cardiovascular events, and pure red cell aplasia (PRCA). In this study, we have analysed a case report of allergic reactions to Erythropoietin, in addition to pertinent published reviews and research publications.



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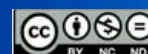
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Available online 1 September 2025

Case report:

A 65-year-old female, diagnosed with anaemia due to chronic kidney disease, received a prescription for subcutaneous injections of Erythropoietin 4000 IU, administered once every two weeks. Following her second dose, she developed erythematous polymorphous eruptions on her palms, hands, legs, and abdomen. Within two days, she experienced fever and joint pain. Notably, there were no signs of oral mucosal involvement, and her medical history did not reveal any other significant conditions. The patient was on other medications like ferrous sulphate, calcium carbonate and cilnidipine 20 mg.



Fig. 1: Erythematous polymorphous "target" lesions of EM



Fig. 2: Erythematous patches seen over stomach

The Fig. 1 and Fig. 2 represents the symptoms of disease. Discontinuation of the drug was recommended due to suspected delayed allergic reaction to erythropoietin. The patient was subsequently referred to a dermatologist for further evaluation and management. Diagnosis of erythropoietin induced erythema multiforme was done. Laboratory investigations showed Haemoglobin 7.4 g/dL (13.00-18.00), serum urea and serum creatinine. Patient improved completely with conservative management of iv corticosteroids, antihistaminics and emollients over a few weeks.

Discussion

Erythropoietin is commonly prescribed for situations where the body is unable to produce enough red blood cells. The two main uses approved by the FDA are treating anaemia caused by chronic kidney disease and managing anaemia that results from chemotherapy in cancer patients (Schoener et al., 2023). Erythropoietin can also be used to prevent or treat anaemia resulting from surgery or medications (e.g., zidovudine) used for other conditions like HIV or cancer. The recommended starting dose for adult patients is 50 to 100 Units/kg 3 times per week subcutaneously.

Anaemia in chronic kidney disease is primarily caused by reduced erythropoietin production, iron and vitamin deficiencies, chronic inflammation, blood loss, uremic toxins, and bone marrow suppression (Shaikh et al., 2023). In chronic kidney disease (CKD), erythropoietin stimulates the bone marrow to produce red blood cells, countering the reduced natural erythropoietin production due to kidney impairment. Administering synthetic erythropoietin helps alleviate anaemia, improve oxygen transport, and enhance the quality of life for CKD patients (Hayat et al., 2008).

In instances of hypersensitivity to erythropoietin, allergic reactions are categorized into immediate and delayed types (Rueangsri et al., 2023). Delayed type reactions may manifest as various skin issues, including pruritic maculopapular rash, exfoliative dermatitis, drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP), with varying severity documented.

Erythema multiforme (EM) is an acute inflammatory, mucocutaneous, psychosomatic, and vesiculobullous condition that ranges from minor to major forms (Shivhare et al., 2023). The term "multiforme" refers to its diverse clinical manifestations, which include macules, papules, vesicles, and ulcers. The hallmark of this disease is the acral distribution of target lesions, characterized by concentric rings with a darker center. These lesions can be typical (three concentric rings) or atypical (two concentric rings). Based on mucous membrane involvement, EM is classified into EM minor (without mucosal involvement) and EM major (with mucosal involvement). The most commonly affected mucosal sites are the lips, tongue, and oral mucosa, though ocular and genital mucous membrane involvement has also been reported. EM was once considered part of the spectrum including Stevens-Johnson syndrome and toxic epidermal necrolysis; however, studies have demonstrated that these conditions are significantly distinct and should not be grouped together (Hafsi et al., 2023).

EM has a multifactorial etiology, with most cases (90%) triggered by infections, particularly herpes simplex virus (HSV-1/2). Drug-induced EM accounts for less than 10%

of cases (Shivhare et al., 2023). Drug induced Erythema Multiforme (DIEM) or in this case, Erythropoietin induced erythema multiforme is rarest and lesser known variant of EM. Our case shows no mucosal involvement, so its categorized as atypical variant of EM minor. The adverse drug event was evaluated using the WHO-UMC scale (Parida et al., 2013) and determined to be "Probable/Likely." Similarly, according to the Naranjo scale (Murayama et al., 2018), it was classified as "Probable."

As erythropoietin is a first line agent of treatment in advanced stages of Chronic Kidney Disease, this case report cautions us about judicious use of various erythropoietin congeners in patients having history of drug induced allergic reactions (Macdougall et al., 2024). Drug-induced erythema multiforme is a less frequently reported form of EM, with the primary causative agents being NSAIDs, antibiotics, and anticonvulsants (Aswath et al., 2022).

Conclusion

Erythropoietin Induced EM is the rarest recorded presentation of Erythema Multiforme till date. A temporal relationship exists between recent subcutaneous administration of erythropoietin and the appearance of symptoms of EM. Extreme caution should be taken while prescribing Erythropoietin therapy in patients with past h/o of any hypersensitivity reaction. Erythropoietin should be offered meticulously to patients with anaemia in CKD, considering its benefit in terms of quality of life and physical function, especially in patients considered for transplantation

Conflict of Interest

Authors declared no conflict of interest.

Acknowledgement

We thank the Indian Pharmacopoeia commission for providing a platform to detect and monitor this case as reported.

References

Aswath, N., & Rakshana, R. (2022). Drug induced erythema multiforme of the oral cavity. *Archive of clinical cases*, 9(4), 157–160. <https://doi.org/10.22551/2022.37.0904.10224>

Hafsi W, Badri T. Erythema Multiforme. [Updated 2023 May 27]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK470259/>

Hayat, A., Haria, D., & Salifu, M. O. (2008). Erythropoietin stimulating agents in the management of anemia of chronic kidney disease. *Patient preference and adherence*, 2, 195–200. <https://doi.org/10.2147/ppa.s2356>

Macdougall I. C. (2024). Anaemia in CKD-treatment standard. *Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association*, 39(5), 770–777. <https://doi.org/10.1093/ndt/gfad250>

Murayama, H., Sakuma, M., Takahashi, Y., & Morimoto, T. (2018). Improving the assessment of adverse drug reactions using the Naranjo Algorithm in daily practice: The Japan Adverse Drug Events Study. *Pharmacology research & perspectives*, 6(1), e00373. <https://doi.org/10.1002/prp2.373>

Parida S. (2013). Clinical causality assessment for adverse drug reactions. *Indian journal of anaesthesia*, 57(3), 325–326. <https://doi.org/10.4103/0019-5049.115608>

Rueangsri, R., & Laisuan, W. (2023). Epoetin-alfa induced pruritic maculopapular eruption: Case report and literature review. *Asian Pacific journal of allergy and immunology*, 41(3), 231–235. <https://doi.org/10.12932/AP-040719-0592>

Schoener B, Borger J. Erythropoietin Stimulating Agents. [Updated 2023 Mar 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK536997/>

Shaikh H, Hashmi MF, Aeddula NR. Anemia of Chronic Renal Disease. [Updated 2023 Feb 24]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK539871/>

Shivhare, P., Haidry, N., Sharma, A., Agrawal, D., Gupta, A., & Subramanyam, S. (2023). Drug-Induced Erythema Multiforme. *Case reports in dermatological medicine*, 2023, 8706006. <https://doi.org/10.1155/2023/8706006>